Biochemical and Biophysical Research Communications 2004 vol.314 N2, pages 550-554

Cytotoxicity of RNases is increased by cationization and counteracted by KCa channels

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Abstract

KCa channels are involved in control of cell proliferation and differentiation. Here we have revealed their role in overcoming the RNase-induced cytotoxicity. Toxic effects of Streptomyces aureofaciens RNases Sa, Sa2, Sa3, and of RNase Sa charge reversal mutants on the human embryonic kidney cell lines differing only by the presence of KCa channels were characterized. In contrast to other RNases, a basic variant of RNase Sa and RNase Sa3 exhibit significant cytotoxic activity of the same order of magnitude as onconase. Our data indicate the absence of a correlation between catalytic activity and stability of RNases and cytotoxicity. On the other hand, cationization enhances toxic effect of an RNase indicating the major role of a positive charge. Essentially lower sensitivity to cytotoxic microbial RNases of cells expressing KCa channels was found. These results suggest that cells without the KCa channel activity cannot counteract toxic effect of RNases.

http://dx.doi.org/10.1016/j.bbrc.2003.12.110

Keywords

Charge reversal mutants, Cytotoxicity, Human embryonic kidney cells, KCa channels, Ribonuclease Sa